8. (Amended) A method of [claims] claim 3, wherein [the] removing the complex-labeled cells is accomplished by a magnetic field acting on the magnetic particles.

9. (Amended) A method of claim 2, further comprising:
separating CD4+ cells from the sample prior to said contacting.

10. (Amended) A method of claim 2, further comprising:
separating CD8+ cells from the sample prior to said contacting.

12. (Amended) A method of claim 1, wherein the [tissue is lymphoid] resting lymphoid mononuclear cells are obtained from a lymphoid tissue.

Cancel claim 14 without prejudice or disclaimer.

REMARKS

The oath has been objected to on the grounds that it does not state that all information "material to patentability" has been disclosed. This objection is not understood. The oath, as filed, states that the inventors "acknowledge the duty to disclose information which is material to examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a)." (Emphasis added.) Thus, the inventors have directly acknowledged the Duty of Disclosure referred to by the statute. If anything, the term "material to examination" recited in the oath is broader than the term "patentability" used in the statute and is therefore supernumerary, not discordant.

As for the objection to the grammatical tense, it is clear that the examples are in the present tense. The only lapse appears in Example 3 which has been corrected. [It is noted that M.P.E.P citation 608.01(b) cited in the Office Action is for Abstracts, although the abstract has not been objected to.]

Claims 2, 6-8, and 10 have been corrected deleting the use of plural "claims."

Rejection Under 37 U.S.C. §112, First Paragraph

The cell lines recited in Claim 16 are well-known and readily available to the public. For example: the Jurkat cell line is cited in at least 1027 patents (Exhibit 1); the U1 cell line is cited in at least 340 patents (Exhibit 2); the OM-10.1 cell line is cited in at least 20 patents and is available from the ATCC (Exhibit 3). Thus, deposit by Applicant is unnecessary. See, M.P.E.P. §2404.01.

Rejection Under 35 U.S.C. §112, Second Paragraph

The term "capable of" has been deleted from claim 1. The term "treating"has been replaced in claims 1 and 14 with the term "contacting."

Claims 2, 9 and 10 has been amended to clarify that the resting cells are obtained "prior to said contacting" in Claim 1, clarifying when the steps are performed. CD4+ and CD8+ cells can be separated by any effective manner, e.g., Specification, Page 5, lines 13-22. Such cells, if not expressing gp120, are resting, and can be separated according to Chun et al., 1995 (e.g., Page 1285, Column 1).

It is stated that Claim 2 is vague and indefinite in the phrase "obtaining sample cell population." It clear from the claims (e.g., 1 and 15) and specification (e.g., Page 4, lines 14-21) that latent viral load can be measured in any cell population, such as primary or cultured cells. Thus, it is not understood why the claim is rejected as not in compliance with §112, second paragraph.

The term "each" in Claim 3 has been clarified by reciting "said antibodies." As far as the terms "labeled cells" and "complex-labeled cells," the "thereby" phrase in steps a) and b) of Claim 3 has been used to indicate that the "labeled cells" are formed by attaching gp120-specific antibodies to cells and that the "complex-labeled cells" are formed by attaching a capture-moiety specific antibody to the labeled cells. Applicant believes that this clear, especially when read in light of the specification; however, if the examiner has an alternative suggestion, please provide it.

The term "capture moiety" is defined in the specification, e.g., on Page 11, lines 21-29.

Claim 5 has been amended by replacing the term "bead" with "particle" to make the claim consistent with the other pending claims.

Claim 8 has been amended to clarify that the "removing" is "removing the complex-labeled cells."

Claim 12 has been amended to clarify that the resting lymphoid cells are obtained from a lymphoid tissue.

Rejection Under 35 U.S.C. §103

Claims 1-16 are rejected under 35 U.S.C. §103 as allegedly unpatentable over Chun et al., *Nature*, 387:183-188, 1997, in view of Chun et al., *Nature Medicine*, 1:1284-1290, 1995, and Essex et al., U.S. Pat. No. 4,725,669, and further in view of Chun et al., *Journal of Experimental Medicine*, 188:83-91, 1998.

It is stated in the Office Action that "Chun et al. differs from the recited claims in that they do not used anti-gp120 coupled to magnetic beads for the depletion of cells actively infected with HIV or [sic] do they use the appearance of gp120 on the 'stimulated' resting cells as the indicator of virus production." Office Action dated February 25, 2000, Paper No. 5, Page 8.

These results of Chun et al. (e.g., 1995, 1997, and 1998 references) do not alone, or, in combination, e.g., with Essex et al., disclose or suggest the present invention. For example, in Chun, 1995, after action with PHA, the latently infected cells were tested for the ability to produce p24, an *intracellular* antigen. See, e.g., Chun et al., 1995, Page 1287, Column 1, lines 1-8. The amounts of p24 per unit volume were determined but no correlation was made between these amounts and cell number. Instead, only picograms (pg) per milliliter (ml) were determined. See, e.g., Chun et al., 1995, Fig. 3b. Thus, there is no detecting the expression of cell-surface gp120 on intact cells and no determining the number therein.

not a limitation of claims

In Chun et al., 1997, the authors utilized a "quantitative viral culture" to determine the fraction of cells that can be induced to produce infectious virus. See, e.g., Chun et al., 1997, Page 185, Column 1, second paragraph. This assay involves collecting supernatant from the activated cells, incubating purified resting T-cells with the supernatant, and then determining whether such supernatant contain virus particles by measuring its ability to infect the resting T-cells. Not only is this assay complicated and labor-intensive, but it also does not provide a direct measure of the number of latently infected cells. It measures the

ability of activated latently infected cells to produce viral particles which are subsequently used to infect another cell population. As Chun et al. describe it, the "frequency" of actually infected cells is derived from complicated statistical methods. See, e.g., Chun et al., 1997, Page 187, "Culture studies"; "Mathematical and statistical methods"; Page 184, Figure 2.

The deficiencies in the Chun references are not simply a failure to measure gp120, but also, e.g., a failure to determine numbers of cells expressing cell-surface gp120. Instead, they use an indirect, statistical frequency value. The numbers of cells expressing cell-surface gp120 significantly, and unexpectedly, provides a new value for assessing the status of the disease. For instance, this value can be referred to as a unit of infectivity since, upon activation of the dormant virus, such cell has the ability to infect other cells. See, e.g., Specification, Page 3, lines 7-15. Units of infectivity are a more meaningful characterization of latent viral load that the statistical value derived by Chun et al., and provides a more accurate description of the patient's disease status. The Chun references fail to have appreciated this.

It is known in the art that there are various indices of HIV infection, such as infectious viral particles, viral nucleic acid (*e.g.*, pol, gag, nef, etc.), p24, gp120, gp41, gp160, etc. However, such knowledge does not suggest that any one of such indices would be useful for measuring latent viral load. In this light, Essex et al., and any other reference teaching gp120, is entirely irrelevant since they disclose it for conventional assays. [Essex et al., in particular, is not relevant since they only look at gp120 after it has been extracted from the cells. See, e.g., Essex et al., Column 3, lines 19-24.] In fact, the Chun references teach away from the present invention since when they go to assess latent virus they chose the intracellular p24 antigen and infectious virus, not a cell-surface antigen such as gp120. This teaching away is even more pronounced when combined with Essex et al. who teach lysing cells prior to measuring gp120, not detecting the expression of cell surface gp120 on intact cells.

A proper analysis under §103 requires, *inter alia,* consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of

ordinary skill would have a reasonable expectation of success. *See* In re Dow Chemical Co.,5 USPQ2d 1529, 1531 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure. In re Vaeck, 20 USPQ2d 1438 (Fed. Cir. 1991). Here, the PTO has failed to provide any motivation to have combined the references to have arrived at the present invention.

Respectfully submitted,

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